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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/258,132	02/26/1999	PHILIP GOELET	04990.0007.U	3407

7590 10/15/2010

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EXAMINER	
MYERS, CARLA J	

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
10/15/2010	PAPER

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The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte PHILIP GOELET, MICHAEL R. KNAPP, and
STEPHEN ANDERSON

Appeal 2009-009122
Application 09/258,132
Technology Center 1600

Before ERIC GRIMES, FRANCISCO C. PRATS, and
JEFFREY N. FREDMAN, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL[1]

This is an appeal under 35 U.S.C. § 134 involving claims to a method of identifying bases in a nucleotide sequence. The Examiner has rejected the

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

claims as obvious over the prior art. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

Claims 64 and 66-71 are on appeal. The claims have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). Claim 64 is representative and reads as follows:

64. A method of determining the identity of one or more nucleotide bases at a plurality of specific positions in one or more nucleic acid molecules of interest, comprising:

(a) treating a sample comprising the one or more nucleic acid molecules of interest, if the nucleic acid molecules of interest comprise double-stranded nucleic acid, so as to obtain unpaired nucleotide bases spanning the specific positions, or directly employing a sample comprising the one or more nucleic acid molecules of interest in step (b) if the nucleic acid is singlestranded;

(b) contacting the sample from step (a) with a plurality of different oligonucleotide primers, wherein:

(i) each such different oligonucleotide primer hybridizes, under high stringency hybridization conditions, to a corresponding different stretch of nucleotide bases present in the nucleic acid molecules of interest which is immediately adjacent to the specific position of a nucleotide base to be identified with that oligonucleotide primer, so as to form a duplex such that the nucleotide base to be identified is the first unpaired base of the nucleic acid molecule of interest immediately downstream of the 3' end of the oligonucleotide primer; and

(ii) each different oligonucleotide primer comprises a corresponding different affinity moiety, the oligonucleotide primer comprising the affinity moiety being capable of hybridizing with a nucleic-acid template and undergoing a nucleic acid template-dependent primer extension reaction with terminators of a terminator reagent, the affinity moiety permitting affinity separation of the extended oligonucleotide primer from the terminator reagent;

(c) contacting the duplexes from step (b) with a terminator reagent free of dATP, dCTP, dGTP, and dTTP and comprising four different terminators of a nucleic acid template-dependent primer extension reaction,

each terminator comprising a different detectable label corresponding to the terminator, wherein one of the terminators is complementary to a nucleotide base to be identified by each of the oligonucleotide primers, wherein the contacting is carried out in a primer-extension reaction medium under conditions sufficient to permit a template dependent primer extension reaction which incorporates the complementary terminator onto the 3' end of each of the different oligonucleotide primers to thereby extend the 3' end of each of the oligonucleotide primers by one terminator;

(d) affinity separating the respective extended oligonucleotide primers from primer-extension reaction medium by causing each of the extended oligonucleotide primers to contact an affinity group attached to a solid support, such affinity group being complementary to the affinity moiety incorporated in the oligonucleotide primer; and

(e) determining the presence and identity of the nucleotide base at each of the respective specific positions in the one or more nucleic acid molecules of interest by detecting the detectable label of the terminator incorporated at the 3' end of each of the affinity separated extended oligonucleotide primers.

The Examiner has rejected all of the claims under 35 U.S.C. § 103(a) as follows: claims 64, 66, 67, 69, and 70 based on either Cohen EP[2] or Cohen FR,[3] combined with Davis[4] (Answer 4); claim 68 based on either Cohen EP or Cohen FR, combined with Davis and Prober[5] (Answer 6); and claim 71 based on either Cohen EP or Cohen FR, combined with Davis and Tabor[6] (Answer 7). We adopt the Examiner's findings regarding the teachings of the prior art (Answer 4-5, 7), and the reasoning supporting her conclusion that the cited references would have made obvious the claimed

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[2] Cohen et al., EP 0 412 883 A1, published Feb. 13, 1991.
[3] Cohen et al., FR 2,650,840, published Feb. 15, 1991.
[4] Davis et al., WO 90/11372, published Oct. 4, 1990.
[5] Prober et al., US 5,332,666, issued July 26, 1994.
[6] Tabor et al., US 4,962,020, issued Oct. 9, 1990.

method (Answer 6, 7, 8). We also agree with the Examiner's response to Appellants' arguments (Answer 8-26), and add the following remarks only for emphasis.

Appellants argue that Cohen FR[7] teaches that its technique has the advantage of not requiring immobilization of a nucleic acid on a membrane, which was required by three previously known techniques for identifying a mutation in a nucleic acid (Appeal Br. 11). Appellants argue that Davis' technique,

> like the previously known techniques distinguished in the Cohen *et al.* patent, involved immobilization of nucleic acid on a membrane. It is submitted, therefore, that the hypothetical combination proposed in the Office Action on appeal would have been understood by persons of ordinary skill in the art as of the effective filing date of the subject application as running directly counter to the teachings of the Cohen *et al.* patent.

(*Id.* at 11-12.)

As the Examiner pointed out (Answer 9), however, Davis expressly teaches that its method has the advantage of allowing analysis of multiple sequences simultaneously (*see* Davis 26: "It . . . is an advantage of the invention that by using unique tails, any number of alleles or loci may be tested for simultaneously."). Thus, a person of ordinary skill in the art would have recognized that, although combining the methods of Cohen FR and Davis would require immobilization of nucleic acid on a membrane, which Cohen FR characterizes as a disadvantage, it would have the

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[7] Both Appellants and the Examiner cite only to Cohen FR, although the Examiner finds that the application to which Cohen EP claims priority is identical to Cohen FR (Answer 4).

offsetting advantage of allowing the method of Cohen FR to determine the identity of multiple nucleic acid positions in a single experiment.

"[A] given course of action often has simultaneous advantages and disadvantages, and this does not necessarily obviate motivation to combine." *Medichem, S.A. v. Rolabo S.L.,* 437 F.3d 1157, 1165 (Fed. Cir. 2006). *See also Winner Int'l Royalty Corp. v. Wang*, 202 F.3d 1340, 1349 n.8 (Fed. Cir. 2000) ("The fact that the motivating benefit comes at the expense of another benefit . . . should not nullify its use as a basis to modify the disclosure of one reference with the teachings of another. Instead, the benefits, both lost and gained, should be weighed against one another."). In this case, we agree with the Examiner that a worker of ordinary skill would have been led to combine the methods disclosed by Cohen FR and Davis in order to gain the advantage of analyzing multiple nucleic acid positions in a single experiment, notwithstanding the need to immobilize nucleic acids on a membrane in order to do so.

SUMMARY

We affirm all of the rejections on appeal: claims 64, 66, 67, 69, and 70 as obvious based on either Cohen EP or Cohen FR, combined with Davis; claim 68 as obvious based on either Cohen EP or Cohen FR, combined with Davis and Prober; and claim 71 as obvious based on either Cohen EP or Cohen FR, combined with Davis and Tabor.

TIME PERIOD FOR RESPONSE

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

cdc

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